

What is claimed is:

Claims

- 1           1.    A method of inhibiting rejection of a  
2   transplanted tissue in a mammal, said method comprising the  
3   steps of  
4               a)    introducing into a cell, either in vivo or  
5   ex vivo, DNA encoding an immunosuppressive polypeptide, and  
6               b)    if step (a) was carried out ex vivo,  
7   transplanting said cell into said mammal  
8               wherein expression of said polypeptide is  
9   regulated by DNA which does not naturally regulate said  
10   expression, so that said polypeptide is expressed close  
11   enough to said transplanted tissue to inhibit rejection.
- 1           2.    A method of inhibiting rejection of a  
2   transplanted tissue in a mammal, said method comprising the  
3   steps of  
4               a)    introducing into a cell, either in vivo or  
5   ex vivo, DNA encoding a glycosidase, and  
6               b)    if step (a) was carried out ex vivo,  
7   transplanting said cell into said mammal  
8               wherein expression of said glycosidase is  
9   regulated by DNA which does not naturally regulate said  
10   expression, so that said polypeptide is expressed close  
11   enough to said transplanted tissue to inhibit rejection.
- 1           3.    The method of claim 1 or claim 2 wherein said  
2   cell is a cell of an allograft.
- 1           4.    The method of claim 1 or claim 2 wherein said  
2   cell is a cell of a xenograft.

1           5. A method of inhibiting a destructive autoimmune  
2 response in a mammal, said method comprising the steps of  
3           a) introducing into a cell, either in vivo or  
4 ex vivo, DNA encoding an immunosuppressive polypeptide, and  
5           b) if step (a) was carried out ex vivo,  
6 transplanting said cell into said mammal  
7           wherein expression of said polypeptide is  
8 regulated by DNA which does not naturally regulate said  
9 expression, so that said polypeptide is expressed close  
10 enough to the site of said destructive autoimmune response  
11 to inhibit destruction.

1           6. The method of claim 5 wherein said mammal is a  
2 mammal with rheumatoid arthritis.

1           7. The method of claim 5 wherein said mammal has  
2 diabetes caused by an autoimmune response.

1           8. The mammal of claim 7, wherein said mammal is  
2 presymptomatic.

1           9. The method of claim 5 wherein said mammal is a  
2 mammal with systemic lupus erythematosus.

1           10. The method of claim 5 wherein said mammal is a  
2 mammal with multiple sclerosis.

1           11. The method of claim 1, 2 or claim 5 wherein  
2 said DNA encodes IL-10.

1           12. The method of claim 1, 2 or 5 wherein said DNA  
2 encodes TGF- $\beta$ .

1           13. The method of claim 1, 2 or claim 5 wherein  
2 said DNA encodes cyclosporine synthetase and said method  
3 further comprises administering to said mammal a  
4 therapeutically effective amount of a cyclosporine  
5 precursor.

1           14. The method of claim 1, 2 or claim 5 wherein  
2 expression of said polypeptide is constitutive.

1           15. The method of claim 1, 2 or claim 5 wherein  
2 expression of said polypeptide is inducible by a compound  
3 that stimulates an immune response.

1           16. The method of claim 1 or claim 5, said DNA  
2 further comprising nucleic acids encoding an indicible  
3 polypeptide which activates expression of said DNA encoding  
4 said immunosuppressive protein, said inducible polypeptide  
5 activating said expression in the presence of a non-toxic  
6 compound.

1           17. The method of claim 1, 2 or 5 wherein  
2 expression of said polypeptide is inducible by a compound  
3 which is tissue specific.

1           18. The method of claim 1, 2 or claim 5, said DNA  
2 comprising regulatory elements including a synthetic  
3 regulatory DNA sequence from at least one of NF-KB, NF-IL-6,  
4 IL-6, LRE, AP-1, p91/stat, or the IL-6 response elements.

1           19. The method of claim 1, 2 or claim 5 wherein  
2 said introducing of said DNA is *in vivo*.

1           20. The method of claim 1, 2 or claim 5 wherein  
2 said introducing of said DNA is *in vitro*.

1           21. The method of claim 1, 2 or 5 wherein said cell  
2 is a cell of the heart.

1           22. The method of claim 1, 2 or 5 wherein said cell  
2 is a cell of the liver.

1           23. The method of claim 1, 2 or 5 wherein said cell  
2 is a cell of the kidney.

1           24. The method of claim 1, 2 or 5 wherein said cell  
2 is a cell of the neuronal tissue.

1           25. The method of claim 1, 2 or 5 wherein said cell  
2 is a cell of the lung.

1           26. The method of claim 1, 2 or 5 wherein said cell  
2 is a cell of the pancreas.

1           27. The method of claim 24 wherein said cell is a  
2 cell of the central nervous system.

1           28. The method of claim 1, 2 or 5 wherein said cell  
2 is a cell of said mammal.

1           29. The method of claim 1, 2 or 5 wherein said cell  
2 is a myoblast.

1           30. The method of claim 1, 2 or 5 wherein said cell  
2 is a renal tubular epithelial cell.

          31. The method of claim 1, 2 or 5 wherein said  
mammal is a human.

1           32. A substantially pure protein characterized in  
2 that  
3           it is secreted by cloned anergic T-cells,  
4           it blocks IL-2 stimulated T-cell proliferation,  
5           it has an apparent molecular weight of between  
6 10 and 30 kilodaltons,  
7           it can be inactivated by heating to 65°C for 15  
8 minutes,  
9           it blocks IL-4 stimulated T-cell proliferation  
10 in vitro,  
11           it is non-cytotoxic to T-cells, and  
12           it does not inhibit the production of IL-2 by  
13 T-cells in vitro.

1           33. A purified nucleic acid encoding the protein of  
2 claim 32.

1           34. A method of altering the effect of IL-2 on an  
2 IL-2 receptor-bearing cell in a mammal, said method  
3 comprising  
4           bringing into close proximity with said cell a  
5 second cell of said mammal which is transfected with the  
6 nucleic acid of claim 33 so that said second cell secretes  
7 said protein.

1           35. The method of claim 34, wherein said second  
2 cell is a T-cell.

1           36. The method of claim 34, wherein said second  
2 cell is an endothelial cell lining a blood vessel.

1           37. The method of claim 34, wherein said second  
2 cell is an epithelial cell.

1           38. The method of claim 37, wherein said epithelial  
2 cell is of the proximal tubule of the kidney.

1           39. The method of claim 38, wherein said epithelial  
2 cell is a gut epithelial cell.

1           40. The method of claim 34, wherein said mammal is  
2 a human.

1           41. A method of altering the effect of IL-2 on an  
2 IL-2 receptor-bearing cell in a mammal, comprising,  
3           transfecting said cell with the nucleic acid of  
4 claim 33 so that said cell secretes said protein.

1           42. A method of altering the effect of IL-4 on an  
2 IL-4 receptor-bearing cell in a mammal, said method  
3 comprising  
4           bringing into close proximity with said cell a  
5 second cell of said mammal which is transfected with the  
6 nucleic acid of claim 33 so that said second cell secretes  
7 said protein.

1           43. The method of claim 42, wherein said second cell  
2 is a T-cell.

1           44. The method of claim 42, wherein said second cell  
2 is an endothelial cell lining a blood vessel.

1           45. The method of claim 42, wherein said second cell  
2 is an epithelial cell.

1           46. The method of claim 45, wherein said epithelial  
2 cell is of the proximal tubule of the kidney.

1           47. The method of claim 45, wherein said epithelial  
2 cell is a gut epithelial cell.

1           48. The method of claim 42, wherein said mammal is  
2 a human.

1           49. A method of altering the effect of IL-4 on an  
2 IL-4 receptor-bearing cell in a mammal, said method  
3 comprising  
4           transfecting said cell with the nucleic acid of  
5 claim 33 so that said cell expresses said protein.

1           50. A human T-cell clone characterized in that it  
2 is anergic;  
3 is dependent on recombinant human IL-2 for  
4 growth;  
5 expresses cell surface CD8;  
6 is non-cytolytic; and,  
7 expresses VB11 T cell receptor.